Fibroblast growth factor 10 plays a causative role in the tracheal cartilage defects in a mouse model of Apert syndrome.

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Public Summary:

Scientific Abstract:
Patients with Apert syndrome (AS) display a wide range of congenital malformations including tracheal stenosis, which is a disease characterized by a uniform cartilaginous sleeve in place of a normally ribbed cartilagenous trachea. We have studied the cellular and molecular basis of this phenotype in a mouse model of AS (Fgfr2c(+/Delta) mice), which shows ectopic expression of Fgfr2b in mesenchymal tissues. Here we report that tracheal stenosis is associated with increased proliferation of mesenchymal cells, where the expression of Fgf10 and its upstream regulators Tbx4 and Tbx5 are abnormally elevated. We show that Fgf10 has a critical inductive role in tracheal stenosis, as genetic knockdown of Fgf10 in Fgfr2c(+/Delta) mice rescues this phenotype. These novel findings demonstrate a regulatory role for Fgf10 in tracheal development and shed more light on the underlying cause of tracheal defects in AS.